



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷: C12N 15/12, 5/10, 1/21, C07K 14/47, 16/18, A61K 38/17, C12Q 1/68		A3	(11) International Publication Number: WO 00/15799 (43) International Publication Date: 23 March 2000 (23.03.00)																																																
(21) International Application Number: PCT/US99/21688 (22) International Filing Date: 17 September 1999 (17.09.99) (30) Priority Data: 60/155,246 17 September 1998 (17.09.98) US 09/158,720 22 September 1998 (22.09.98) US Not furnished 22 September 1998 (22.09.98) US 60/069,391 4 November 1998 (04.11.98) US 60/128,660 8 April 1999 (08.04.99) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications US Not furnished (CIP) Filed on 17 September 1998 (17.09.98) US 09/158,720 (CIP) Filed on 22 September 1998 (22.09.98) US Not furnished (CIP) Filed on 22 September 1998 (22.09.98) US 09/186,815 (CIP) Filed on 4 November 1998 (04.11.98) US 09/156,039 (CIP) Filed on 17 September 1998 (17.09.98) US Not furnished (CIP) Filed on 4 November 1998 (04.11.98) US 60/128,660 (CIP)		Filed on 8 April 1999 (08.04.99) (71) Applicant (for all designated States except US): INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). GORGONE, Gina, A. [US/US]; 1253 Pinecrest Drive, Boulder Creek, CA 95006 (US). PATTERSON, Chandra [US/US]; 490 Sherwood Way #1, Menlo Park, CA 94025 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View, CA 94040 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). AZIMZAI, Yalda [US/US]; 2045 Rock Springs Drive, Hayward, CA 94545 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). YANG, Junming [CN/US]; 7136 Clarendon Street, San Jose, CA 95129 (US). (74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 13 July 2000 (13.07.00)																																																	
(54) Title: RNA-ASSOCIATED PROTEINS																																																			
(57) Abstract The invention provides human RNA-associated proteins (RNAAP) and polynucleotides which identify and encode RNAAP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonist. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of RNAAP.																																																			
<table border="0"><tr><td>1</td><td>MSRYLAPFHTSLFVADVADDTASEDLAREF</td><td>399701</td></tr><tr><td>1</td><td>MSRYLAPFHTSLFVADVADDTASEDLAREF</td><td>GI 2961149</td></tr><tr><td>31</td><td>GRYGPIVGVVFLDFFYTRKFRGFAIVQFED</td><td>399701</td></tr><tr><td>31</td><td>GRYGPIVGVVFLDFFYTRKFRGFAIVQFED</td><td>GI 2961149</td></tr><tr><td>61</td><td>VRDASDALHLDRAKHCIGRQIEIQPAGGDR</td><td>399701</td></tr><tr><td>61</td><td>VRDASDALHLDRAKHCIGRQIEIQPAGGDR</td><td>GI 2961149</td></tr><tr><td>91</td><td>KTFNQKAKKGRHVYSSRYDDYDTRHRSR</td><td>399701</td></tr><tr><td>91</td><td>KTFNQKAKKGRHVYSSRYDDYDTRHRSR</td><td>GI 2961149</td></tr><tr><td>121</td><td>SRSYKRRSRSRSDYHARSYSPRHSRFF</td><td>399701</td></tr><tr><td>121</td><td>SRSYKRRSRSRSDYHARSYSPRHSRFF</td><td>GI 2961149</td></tr><tr><td>151</td><td>GRPRRKAFTYHIDQYAGYFSTVLLTTEG</td><td>399701</td></tr><tr><td>151</td><td>GRPRRKAFTYHIDQYAGYFSTVLLTTEG</td><td>GI 2961149</td></tr><tr><td>181</td><td>ERSHSGKRTKEGQPRKPKGGHKLQYE</td><td>399701</td></tr><tr><td>181</td><td>ERSHSGKRTKEGQPRKPKGGHKLQYE</td><td>GI 2961149</td></tr><tr><td>209</td><td>CTNYLTLY</td><td>399701</td></tr><tr><td>170</td><td>YLYSRRRT</td><td>GI 2961149</td></tr></table>				1	MSRYLAPFHTSLFVADVADDTASEDLAREF	399701	1	MSRYLAPFHTSLFVADVADDTASEDLAREF	GI 2961149	31	GRYGPIVGVVFLDFFYTRKFRGFAIVQFED	399701	31	GRYGPIVGVVFLDFFYTRKFRGFAIVQFED	GI 2961149	61	VRDASDALHLDRAKHCIGRQIEIQPAGGDR	399701	61	VRDASDALHLDRAKHCIGRQIEIQPAGGDR	GI 2961149	91	KTFNQKAKKGRHVYSSRYDDYDTRHRSR	399701	91	KTFNQKAKKGRHVYSSRYDDYDTRHRSR	GI 2961149	121	SRSYKRRSRSRSDYHARSYSPRHSRFF	399701	121	SRSYKRRSRSRSDYHARSYSPRHSRFF	GI 2961149	151	GRPRRKAFTYHIDQYAGYFSTVLLTTEG	399701	151	GRPRRKAFTYHIDQYAGYFSTVLLTTEG	GI 2961149	181	ERSHSGKRTKEGQPRKPKGGHKLQYE	399701	181	ERSHSGKRTKEGQPRKPKGGHKLQYE	GI 2961149	209	CTNYLTLY	399701	170	YLYSRRRT	GI 2961149
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EE	Estonia						

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PF-0600 PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 99/ 21688	International filing date (day/month/year) 17/09/1999	(Earliest) Priority Date (day/month/year) 17/09/1998
Applicant INCYTE PHARMACEUTICALS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

Application No
PCT/US 99/21688

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N5/10 C12N1/21 C07K14/47 C07K16/18
A61K38/17 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMHUM1 [Online] E.M.B.L. Databases Accession Number: AF047448, 17 March 1998 (1998-03-17) YANG L ET AL: "Homo sapiens TLS-associated protein TASR mRNA, complete cds" XP002128498 99.5% identity in 621 bp overlap with SeqIdNo.26 / 100% identity in 155 aa overlap with SeqIdNo.1 abstract	1-16,19
P,X	-& YANG L ET AL: "Oncoprotein TLS interacts with serine-arginine proteins involved in RNA splicing" JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 273, no. 43, 23 October 1998 (1998-10-23), pages 27761-27764, XP002128497 the whole document -/--	1-16,19

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *-&* document member of the same patent family

Date of the actual completion of the international search

24 January 2000

Date of mailing of the international search report

02.05.2000

Name and mailing address of the ISA

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Authorized officer

Lonnoy, 0

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/21688

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	--- EP 0 679 716 A (MATSUBARA KENICHI ;OKUBO KOUSAKU (JP)) 2 November 1995 (1995-11-02) Human gene signature HUMGS00127 (SeqIdNo.113): 98.9% identity in 349 bp overlap with SeqIdNo.26	3-11
X	-& DATABASE GENESEQ [Online] E.M.B.L. Databases Accession Number: T19113, 4 July 1996 (1996-07-04) MATSUBARA K ET AL: "Human gene signature HUMGS00127" XP002128499 98.9% identity in 349 bp overlap with SeqIdNo.26 abstract	3-11
A	--- US 5 561 222 A (KEENE JACK D ET AL) 1 October 1996 (1996-10-01) figure 6	
A	--- WO 98 23744 A (INCYTE PHARMA INC ;BANDMAN OLGA (US); GOLI SURYA K (US)) 4 June 1998 (1998-06-04) -----	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 21688

B x I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see additional sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-20 (all partially)

A substantially purified polypeptide of SeqIdNo.1, a fragment of said polypeptide; an isolated and purified polynucleotide encoding said polypeptide, a variant polynucleotide having at least 90% sequence identity to said polynucleotide, a polynucleotide hybridising to said polynucleotide, a polynucleotide having a sequence complementary to said polynucleotide; a detection method using said complementary polynucleotide; a polynucleotide comprising a sequence of SeqIdNo.18 or a fragment thereof, a polynucleotide having at least 90% sequence identity to said polynucleotide of SeqIdNo.18, a polynucleotide complementary to said polynucleotide of SeqIdNo.18; expression vector, host and recombinant method related thereto; a pharmaceutical composition comprising said polypeptide of SeqIdNo.1; an antibody to said polypeptide of SeqIdNo.1 or fragment of said polypeptide of SeqIdNo.1; an agonist to said polypeptide of SeqIdNo.1; an antagonist to said polypeptide of SeqIdNo.1; therapeutic application thereof

Inventions 2-17: claims 1-20 (all partially)

Idem as for subject 1 but limited to each of the polypeptide sequences as in SeqIdNo.2-17 and the corresponding polynucleotide sequences as in SeqIdNo.19-34, wherein respectively invention 2 is limited to SeqIdNo.2 and SeqIdNo.19, invention 3 is limited to SeqIdNo.3 and SeqIdNo.20,..., invention 17 is limited to SeqIdNo.17 and SeqIdNo.34.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 3.

Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 17,18,20

Claims 17, 18 and 20 refer to an agonist, an antagonist and to the use of an antagonist of the polypeptide of claim 1 without giving a true technical characterization. Moreover, no such compound is defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such speculative claims the wording of which is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/21688

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0679716	A	02-11-1995	AU 8116494 A	13-06-1995
			CA 2153480 A	01-06-1995
			WO 9514772 A	01-06-1995

US 5561222	A	01-10-1996	US 5866680 A	02-02-1999

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			AU 7410598 A	22-06-1998
